Remarks

Reconsideration of this Application is respectfully requested. Upon entry of the foregoing amendment, claims 16-20 and 39-49 are pending in the application, with claims 16 and 19 being the independent claims. Claims 42 and 43 are sought to be amended. Support for these amendments can be found in previously presented claims 42 and 43. New claim 49 is sought to be added. Support for the new claim can be found in the specification, for example, at Figure 8; Example 3 at pages 42-45; and page 29, paragraph 79 ("The building block amino acid is N_{α}-*Fmoc*-N_{ε}-TMR-Lysine, which is also blocked by FMOC, and can be obtained from many vendors, including Molecular Probes, (Eugene, OR, Catalogue No. F-11830)." *See also* Exhibit A. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Response to Election of Species Requirement

In reply to the Office Action dated July 20, 2004, requiring election of a species, Applicants hereby provisionally elect to prosecute the marker molecule species wherein the molecule is the peptide having SEQ ID NO: 3 labeled at its lysines with TMR, wherein the protein and/or nucleic acid of known molecular weight is MBP-95aa, and wherein the peptide having SEQ ID NO: 3 is ligated via a peptide bond through its N-terminal cysteine to the C-terminal end of MBP-95aa. To the extent necessary, the species MBP-95aa-CO-S-CH_2-CH_2-SO_3Na is elected as the protein and/or nucleic acid of known molecular weight that is ligated to SEQ ID NO: 3 in the method of making a marker molecule.

The description which follows constitutes a species election of a fully defined marker molecule with all atoms in that molecule accounted for. The description which

follows also constitutes a species election of the components used in the method of preparing a marker molecule, with all atoms in those components accounted for. Claims 16, 19, 39-43, 48 and 49 read on the elected species.

I. Election of a Specific Protein and/or Nucleic Acid of Known Molecular Weight

Applicants elect the species MBP-95aa-CO-S-CH_2-CH_2-SO_3Na as the protein and/or nucleic acid of known molecular weight. MBP-95aa is a recombinant fragment corresponding to amino acids 1-92 of the 404 amino acid-long E. coli maltose binding protein (MBP), modified at its C-terminus with Met-Arg-Met. *See* Specification, page 35, paragraph 90. Hence, 92 amino acid residues of MBP combined with the Met-Arg-Met C-terminus modification results in MBP-95aa.

In this election, the α-thioester of claim 16, or the C_α-thioester of claim 19 are present on MBP-95aa-CO-S-CH_2-CH_2-SO_3Na. The α-thioester (or C_α-thioester) is removed upon reaction with the N-terminal cysteine of TMR-labeled SEQ ID NO: 3. The Specification describes a process wherein MBP-95aa-CO-S-CH_2-CH_2-SO_3Na is eluted and subsequently attached to the peptide having SEQ ID NO: 3. *See* Specification, page 35, paragraph 90; page 42, paragraph 112; and Figure 8.

II. Election of a Specific Molecule

Applicants have elected TMR-labeled SEQ ID NO: 3 as the specific molecule. In this election, the thiol-containing moiety of claim 16, or the amino-terminal cysteine residue of claim 19 are the same (i.e., the amino-terminal cysteine of SEQ ID NO: 3).

III. Definition of TMR Labels

The TMR labels are attached to SEQ ID NO: 3's lysine residues via the lysines' epsilon nitrogens. This is evident from Applicants' specification at page 29, paragraph

79, which describes the labeled lysines used in the synthesis of the molecule. This paragraph makes reference to Molecular Probes product F11830 (used in the synthesis), a description of which has been included as Exhibit A. Exhibit A shows that the lysines' epsilon nitrogens are connected to TMR via an amide linkage. Thus, Applicants elect SEQ ID NO: 3 wherein its lysines' epsilon nitrogens are part of an amide bond connected to TMR, as shown in Exhibit A.

IV. Ligating SEQ ID NO: 3 to MBP-95aa- CO-S-CH_2-CH_2-SO_3Na

In the specifically elected marker molecule, SEQ ID NO: 3 is attached to MBP-95aa via a peptide linkage. In particular, the N-terminal cysteine of SEQ ID NO: 3 forms a peptide linkage with the carboxyl terminus of MBP-95aa, as shown in Figure 8. As described above, this peptidyl linkage is made when the N-terminal cysteine residue reacts with the C_α-thioester (or α-thioester) of MBP-95aa-CO-S-CH_2-CH_2-SO_3Na.

Conclusion

This election is made without prejudice to or disclaimer of the other claims or inventions disclosed. This election is made with traverse. Reconsideration and withdrawal of the election of species requirement and prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: August 20, 2004

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Structure for F11830

N^{α}-(9-fluorenylmethoxycarbonyl)-N^{ϵ}-tetramethylrhodamine-(5-carbonyl)-L-lysine (α-FMOC-ϵ-TMR-L-lysine)

Molecular Formula: $C_{46}H_{44}N_4O_8$

Molecular Weight: 780.88

CAS Number/Name: N/A